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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/202,984	03/19/1999	ARMIN PETER CZERNILOFSKY	0652.1830000	3631

7590 10/04/2005

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EXAMINER	
CHUNDURU, SURYAPRABHA	
ART UNIT	PAPER NUMBER
1637	

DATE MAILED: 10/04/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/202,984	CZERNILOFSKY ET AL.	
	Examiner	Art Unit	
	Suryaprabha Chunduru	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 July 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *61,63-90 and 92-120* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *61,63-90 and 92-120* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on July 13, 2005, 2005 has been entered.

Status of the Application

2. The action is in response to the RCE filed on July 13, 2005. Currently claims 61, 63-90, 92-120 are pending. Claims 1-60, 62 and 91 are cancelled. All arguments and amendment have been fully considered and thoroughly reviewed and deemed persuasive in view of the amendment.

Priority

3. This application filed on January 2, 2002, is a 371 of PCT/EP97/03329 filed on 6/25/1997, which claims foreign priority to EP 96/110459 filed on 6/28/1996.

New Grounds of Rejections

Claim Rejections - 35 USC § 102

4. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 61, 63-64, 67-71, 74-85, 87-90, 92-93, 96-100, 103-114, 116-120 are rejected under 35 U.S.C. 102(e) as being anticipated by Brann (WO 95/02823).

Brann teaches high throughput parallel screening method (multiple receptor-format) of claims 61, 90, of determining the pharmacological effect of a substance (test substance) on the activity of different biological target molecules (more than one receptor molecules, multiple receptor format) contained in test cells of same type (see page 9, line 1-5, page 25, line 14-30, page 27, line 10-20), comprising

(a) applying or contacting a test substance in appropriate concentration in one operation (simultaneously) to test cells of the same type comprising more than one cellular substrates (receptors), which differ in that they contain different target molecules (different receptors) (see page 9, line 1-5, page 16, line 10-25, page 23, line 28-34, page 24, line 1-13, page 25, line 14-23 indicating test cells comprising more than one cellular substrate, which are different from one another);

(b) measuring the effect of the substance on the biological activities of said different target molecules using a detection system using different assays or assay format for each substrate (see page 24, line 28-35, page 25, line 1-13, line 24-30);

(c) directly or indirectly comparing the effect of said test substance on the biological activities of said different target molecules, wherein target molecules comprise receptor-coupled signal transduction pathway (see page 24, line 14-27, page 28, line 4-18, page 52, line 13-22).

With regard to claims 63-64, 67-71, 74-76, 92-93, 96-100,103-105, Brann teaches that said different target molecules include Ras, tyrosine kinase receptors serotonin receptors, human growth hormone receptors, neurokinin receptors 1,2 (tachykinin receptors) EGF etc. (see page 24, line 14-27, page 10, line 10-31, page 11, line 1-28);

With regard to claims 77-80, 106-109, Brann teaches that the biological activity is a pathological effect including proliferation, or apoptosis (see page 20, line 1-13, page 25, line 24-26, page 26, line 12-14, page 52, line 13-26, indicating cell growth amplification or inhibition);

With regard to claims 87-89, 116-120, Brann teaches that said test cells are mammalian cells (same or different cells) comprising human cells having same genotype and tumor cells (see page 16, line 10-25, page 11, line 20-25);

With regard to claims 81-82, 110-111, Brann teaches that said test cells are transformed with DNA operable encoding said different target molecules, which include receptors (see page 15, line 3-31);

With regard to claims 83-85, 112-114, Brann teaches said detection system comprises reporter gene expression system comprising luciferase (seepage 24, line 28-35, page 25, line 1-13).

Thus the disclosure of Brann meets the limitations in the instant claims.

Claim Rejections - 35 USC § 103

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out

the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

A. Claims 86 and 115 are rejected under 35 U.S.C. 103(a) as being unpatentable over Brann (WO 95/02823) in view of Chalfie et al. (USPN.5,491,084).

Brann teaches a high throughput parallel screening method as discussed in the section 4 above.

Brann did not teach green fluorescent protein as a reporter gene.

Chalfie et al. teach a method for cells expressing a biological activity (gene expression) of a particular target molecule, wherein the regulatory sequences of a target molecule are linked to a reporter fluorescent protein which fluoresces when said target is expressed within the cells (see column 1, lines 38-52). Chalfie et al. also teach that said reporter fluorescent protein is a gene encoding a green fluorescent protein (column 1, lines 38-41).

Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to combine the method of determining the effect of a substance on the biological activities on target molecules as taught by Brann with the method of detecting effect of a substance on different target molecules linked to a GFP reporter gene system as taught by Chalfie et al. to achieve an enhanced sensitivity in determining the effect of a substance on the biological activity or activities because Chalfie et al. taught that the biological activity of a particular target molecule in response to an external stimulus can be monitored within the cells containing the target by the expression of green fluorescence protein linked to said target and the cells expressing the GFP can be easily selected and sorted by a fluorescent-activated sorter (see

column 4, lines 3-12). Therefore an ordinary practitioner would have motivated to combine the reporter gene mediated detection method of determining the effect of a substance on the biological activity as taught by Brann with the method of selecting or localizing a biological activity within the cells using the reporter gene encoding a green fluorescent protein as taught by Chalfie et al. to enhance the detection of the biological activity of a target molecule within the cells, so as to detect and sort the cells expressing the target molecules without lysing the cells.

B. Claims 65, and 94 are rejected under 35 U.S.C. 103(a) as being unpatentable over Brann (WO 95/02823) in view of Reed et al. (USPN. 5,686,595).

Brann teaches a high throughput parallel screening method as discussed in the section 4 above.

However, Brann did not teach other target molecules which include Bcl-2.

Reed et al. teach a method for screening agents that inhibit binding of Bcl-2 related polypeptide with Bcl-2 target molecule (see column8, lines 15-27), Reed et al. also teach regulation of Bcl-2 expression by modulating the binding properties of Bcl-2 with Bcl-2-related agents in cancer cells would reduce the level of free Bcl-2 in a cell and modulate the susceptibility of a cell to apoptosis (see column 24-49).

Therefore an ordinary practitioner would have been motivated to combine the method of detecting the effect of a substance on the biological activity of different target molecules as taught by Brann with the different target molecules as taught by Reed et al. to achieve in developing an improved and method for detecting the effect of a substance on a wide range of target molecules that affect not only cell proliferation activity but also apoptosis activity because Reed et al. taught the advantage of monitoring Bcl-2 expression in apoptosis which

enables to discover pharmacologically active substances that modulate the expression of Bcl-2 and apoptosis (see column 11, lines 45-49). An ordinary practitioner would have been motivated to combine the method of detecting the effect of a substance on the biological activity of different target molecules of Brann with inclusion of Bcl-2 target molecule which would result in improving the method of detecting the effect of a substance on not only the biological activity related to cell proliferation but also the effect of a substance on the biological activity related to apoptosis which would also aid in identifying drug targets related to apoptosis.

C. Claims 66, 72-73, 95, 101-102 are rejected under 35 U.S.C. 103(a) as being unpatentable over Brann (WO 95/02823) in view of Brown et al. (USPN. 5,929,081).

Brann teaches a high throughput parallel screening method as discussed in the section 4 above.

However, Brann did not teach target molecules which include HER , KDR, Raf receptors.

Brown et al. teach method for treating diseases mediated by cellular proliferation signal transduction pathway effector molecules, wherein Brown et al. disclose that the method comprises treating the diseases associated with cellular target receptor molecules such as VGEF (kinin domain receptors (KDR)), HER2, 3, ras/Raf pathway signaling molecules (see col. 10, line 13-58).

Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to combine the method of determining the effect of a substance on the biological activities on target molecules as taught by Brann with the receptors for Raf, HER and KDR signaling pathway as taught by Brown et al. to achieve an expected advantage of developing a versatile and sensitive method of detecting the effect of a substance on biological

activities of a wide range of target molecules because Brown et al. explicitly taught that the method of treating diseases mediated by signal transduction pathway receptor molecules (see col.10, line 23-58). An ordinary practioner would have a reasonable expectation of success that the combination of the method taught by Brann with the different receptor target molecules including ras/raf pathway, Her and KDR receptor molecules as taught by Brown et al. would result in developing an improved and sensitive method for detecting the effect of a substance on various target molecules that activate a signal transduction pathway(s) thereby characterizing said activated target molecules and detecting the corresponding signal transduction pathway mediated by said receptor molecules and such modification of the method is considered as obvious over the cited prior art in the absence of secondary considerations.

Response to arguments:

4. With regard to the rejection maintained in the previous office action under 35 USC 102(e) as anticipated by Vande Wounde et al., Applicants' arguments and amendment are fully considered and the rejection is moot in view of the amendment and new grounds of rejections.

5. With regard to the rejection maintained in the previous office action under 35 USC 102(e) as anticipated by Tang et al., Applicants' arguments and amendment are fully considered and the rejection is moot in view of the amendment and new grounds of rejections.

6. With regard to the rejection maintained in the previous office action under 35 USC 103(a) as being obvious over Vande Wounde et al. in view of Czernilofsky et al., Applicants' arguments and amendment are fully considered and the rejection is moot in view of the amendment and new grounds of rejections.

7. With regard to the rejection maintained in the previous office action under 35 USC 103(a) as being obvious over Vande Wounde et al. in view of Czernilofsky et al. further in view of Chalfie et al., Applicants' arguments and amendment are fully considered and the rejection is moot in view of the amendment and new grounds of rejections.

8. With regard to the rejection maintained in the previous office action under 35 USC 103(a) as being obvious over Vande Wounde et al. in view of Reed et al., Applicants' arguments and amendment are fully considered and the rejection is moot in view of the amendment and new grounds of rejections.

Conclusion

No claims are allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Suryaprabha Chunduru whose telephone number is 571-272-0783. The examiner can normally be reached on 8.30A.M. - 4.30P.M , Mon - Friday,.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on 571-272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR

system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Prabha Chunduru 9/30/05.

Suryaprabha Chunduru
Patent Examiner
Art Unit 1637